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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,805	04/08/2004	Henrik Stender	58418-CIP (48497)	9064

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,805	STENDER, HENRIK	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-12,25-31 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-12,25-31 and 34* is/are rejected.

7)☒ Claim(s) *12 and 25-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 12, 2008 has been entered.

2. Claims 3 and 32-33 have been canceled, claims 1, 4, 12, and 25-30 have been amended, and claim 34 has been added. Claims 1-2, 4-12, 25-31, and 34 are now under consideration. Any rejections and/or objections not reiterated herein have been withdrawn.

3. It is noted that the Remarks of August 12, 2008 have been considered; however, those Remarks are moot in view of the new grounds of rejection set forth below. It is particularly noted that the amended claims no longer include the limitation "all species of the genus Pseudomonas, except for Pseudomonas pertucinogena".

Claim Rejections - 35 USC § 112, second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 12 and 25-31 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12 and 25-31 are indefinite because each of the dependent claims only recites a further limitation on the "use" of the claimed product, without making clear how (or even whether) the product claimed actually differs from that of the preceding claim. The instant claims therefore do not clearly apprise one of skill in the art as to the actual structural features of the claimed products, as would be necessary for the artisan to avoid infringing that which is claimed. Further, it is noted that a proper dependent claim must further limit the claim(s) from which it depends. Accordingly, clarification is required.

Claim Objections

6. Claims 12 and 25-31 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

It is noted that this objection applies to the claims to the extent that they may be drawn to probes/kits that are structural identical to those of the claims from which they depend. It is again noted that the manner in which the claimed products actually differ from those of the claims from which they depend is not may clear by applicant's claim language (see the preceding rejection under 35 USC 112, second paragraph).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-12 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Reeve et al (WO 99/47706 A1 [22 Sept 1999]).

It is noted that the specification at page 13 discloses both "exactly complementary" and "substantially complementary" probes/sequences, and that page 14 of the specification teaches that "By the phrase 'complementary' is meant relatively close relationship between the sequence of the PNA probe and its intended nucleic acid template sequence" (lines 20-21). Accordingly, the broadest reasonable interpretation of the terms "complementary" and "complement" in applicant's claims encompasses, e.g., "substantially complementary" sequences and sequences having a "relatively close relationship" to one another.

Reeve et al teach all possible PNA 10mers as well as subsets thereof, present either in solution or on an array; see pages 4-5, particularly lines 13-21 of page 4; lines 7-13 of page 5). Reeve et al disclose the use of their reagents in sequencing by hybridization, and particularly in determining difference between target and reference sequences (see entire reference, particularly, e.g., pages 2-3). The reagents taught by Reeve et al include all possible 10mers, and therefore Reeve et al disclose multiple PNA probes meeting both the structural/length requirements and functional requirements (i.e., being complementary to the recited target 23S sequences or sequences complementary thereto) set forth in independent claims 1 and 34. Further, the reagents of Reeve et al could be used to accomplish the intended use of "detection,

identification or quantitation of Pseudomonas." Accordingly, Reeve et al anticipate the claimed invention.

With further regard to claim 2, the compositions taught by Reeve et al further encompass multiple PNA 10mers that are "at least 90% identical" to sequences that would be considered complements of SEQ ID NO: 1 (particularly given the broad definition of "complementary" noted above). Regarding claim 4, the probes of Reeve et al would also be considered by an ordinary artisan to constitute complements and/or variants of SEQ ID NO: 1 encompassed by the claims.

With respect to claims 5-8, Reeve et al disclose that their PNA probes may be labeled by a variety of methods, including, e.g., the use of fluorescent and chemiluminescent labels (see, e.g., page 4, lines 13-19; page 5, lines 1-11; and the Example), and that molecular beacon structures may also be included in their probes (see, e.g., page 5, lines 3-6); it is also noted that it is an inherent property of such probes that they may be considered "self reporting." Regarding claims 9-10, it is noted that Reeve et al also teach embodiments employing arrays of unlabeled probes (see, e.g., the Example, as well as page 5). Regarding claim 11, it is noted that the instant specification does not include a limiting definition for the term "spacer" or "linker," but refers to these components as have the capability of minimizing adverse effects on hybridization (see, e.g., page 10). Thus, the incorporated bases disclosed as improving hybridization in the probes of Reeve et al (see, e.g., pages 4-5) meet the requirements of claim 11. Regarding claim 12, it is noted that the claim is not further limiting with regard to the actual structure of the claimed product, but rather references a particular

intended use. As the probes of Reeve et al could be employed in the in situ hybridization analysis of Pseudomonas, the probes of Reeve et al meet the requirements of the claim.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 25-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reeve et al (WO 99/47706 A1 [22 Sept 1999]) in view of Ahern et al (The Scientist 9(15):20 [July 1995]).

Reeve et al teach all possible PNA 10mers as well as subsets thereof, present either in solution or on an array; see pages 4-5, particularly lines 13-21 of page 4; lines 7-13 of page 5). Reeve et al disclose the use of their reagents in sequencing by hybridization, and particularly in determining difference between target and reference sequences (see entire reference, particularly, e.g., pages 2-3). The reagents taught by Reeve et al include all possible 10mers, and therefore Reeve et al disclose multiple PNA probes meeting both the structural/length requirements and functional requirements (i.e., being complementary to the recited target 23S sequences or sequences complementary thereto) set forth in independent claim 1. Further, the reagents of Reeve et al could be used to accomplish the intended use of "detection, identification or quantitation of Pseudomonas." With particular regard to claims 25-31,

Reeve et al also disclose kits for performing their methods, which kits may include their disclosed probes in solution and/or on arrays (see, e.g., claim 11). As the kits of Reeve et al could be used in any of the assays mentioned in claims 25-31 (i.e., for any of the recited intended uses of the probes/kits), the Reeve et al reference suggests all of the limitations of the claimed kits with the exception of the "directions" as recited in claim 25.

Ahern teaches that premade reagents provided in kit form are convenient and save researchers time and money, and further teaches the inclusion in kits of "detailed instructions to follow" (see p. 4/6). In view of the teachings of Ahern, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the kits suggested by Reeve et al so as to have included therein instructions for use of the enclosed reagents. An ordinary artisan would have been motivated to have made such a modification in order to have allowed an artisan to more readily use the reagents in a correct manner, thereby saving the practitioner time and reagents, as suggested by the teachings of Ahern.

11. Claims 1-2, 4-7, 9-12, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ludwig et al (Applied and Environmental Microbiology 60(9):3236-3244 [9/1994]) in view of Hyldig-Nielsen et al (US 6,169,169 B1 [01/2001]).

It is noted that all of the claims instant encompass PNA probes comprising the preferred sequence SEQ ID NO: 1. In particular, it is noted that dependent claims 2 and 4 recite this sequence (such that it clearly meets the requirements of independent claim 1), and that the specification teaches that the sequence is present in each of the Pseudomonas species recited in independent claims 1 and 34 (see, e.g., Table 1).

Ludwig et al disclose 23S rRNA partial sequences for a variety of Pseudomonas species, each of which includes an RNA sequence corresponding to the reverse complement of instant SEQ ID NO: 1 (see entire reference, particularly Figure 2); thus, Ludwig et al inherently disclose that instant SEQ ID NO: 1 exactly complements the 23S rRNA sequence of a variety of pseudomonads. It is also noted that an inspection of Figure 2 of Ludwig et al reveals that there are sequence differences between all pseudomonads and a variety of other bacterial species at the region corresponding to instant SEQ ID NO: 1 (see Figure 2). Thus, the teachings of Ludwig et al suggest that the region of 23S rRNA corresponding to instant SEQ ID NO: 1 is a suitable target for a genus-specific probe for pseudomonads. However, Ludwig et al do not teach a PNA probe comprising SEQ ID NO: 1.

Hyldig-Nielsen et al disclose PNA probes targeting the 23S rRNA or rDNA sequences of Neisseria gonorrhoeae and Chylamydia trachomatis (see entire reference). Hyldig-Nielsen et al disclose that probe sequences are selected that will hybridize to and identify target organisms of interest (see, e.g., col 4, line 55-col 5, line 24). Hyldig-Nielsen et al further disclose that PNA probes are advantageous as compared to DNA probes for a variety of reasons, e.g., because shorter probes may be used in sensitive assays, because PNA probes "allow greater flexibility in" assay format, and because hybridization can occur "under conditions not favorable for ordinary DNA probes" (see col 2, lines 37-57).

In view of the teachings of Ludwig et al and Hyldig-Nielsen et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was

made to have prepared a PNA probe comprising SEQ ID NO: 1 for use in detecting one or multiple Pseudomonas species. As noted above, Ludwig et al disclose that SEQ ID NO: 1 is the exact complement of 23S sequences of a variety of pseudomonads, and that it is not the exact complement of a variety of other species. Hyldig-Nielsen et al suggest selecting such complementary sequences for use in detecting target sequences of interest, and further suggest a variety of advantages of PNA probes as compared to DNA probes. Thus, an ordinary artisan would have been motivated to have prepared such a probe for the advantage of, and to achieve the predictable result of, preparing a PNA probe that could be used successfully in the specific detection of pseudomonads in a variety of assay formats and hybridization conditions, as suggested by the teachings of Ludwig et al and Hyldig-Nielsen et al. It is also noted that the product suggested by Ludwig et al in view of Hyldig-Nielsen et al could be used by one of skill in the art in a variety of methods "for the detection, identification and/or quantitation of Pseudomonas".

With further regard to claims 2 and 4, it is again noted that Ludwig et al and Hyldig-Nielsen et al suggest PNA probes comprising SEQ ID NO: 1, which probes are encompassed by the claims. Regarding claims 5-7, Hyldig-Nielsen et al suggest a variety of different labels that may be used successfully with PNA probes (see, e.g., col 8, line 19-col 9, line 57), including, e.g., fluorophores, enzymes, conjugates, haptens, luminescent labels, etc. (see col 8, lines 38-41, teaching multiples labels encompassed by claim 6). With further regard to claim 7, it is a property of many of the labels of Hyldig-Nielsen et al that they may be used in such a way as to be "self-reporting," such

that the requirements of the claim are met. (It is noted that the specification teaches at page 9 that beacon probes are simply "examples" of self-indicating probes; thus, the instant claim is not limited to this particular type of self-reporting probe). With regard to claim 9, Hyldig-Nielsen et al also teach unlabeled PNA probes (see, e.g., col 9, line 58-col 10, line 28). Regarding claim 10, Hyldig-Nielsen et al teach PNA probes bound to a solid support (see, e.g., col 19, lines 10-50). Regarding claim 11, Hyldig-Nielsen et al also teach the use of linkers in PNA probes (see, e.g., col 8, lines 19-36 and col 10, lines 29-41). Regarding claim 12, it is noted that the claim is not further limiting with regard to the actual structure of the claimed product, but rather references a particular intended use. As the probes suggested by Ludwig et al in view of Hyldig-Nielsen et al could be employed in the in situ hybridization analysis of Pseudomonas, the probes meet the requirements of the claim.

12. Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ludwig et al in view of Hyldig-Nielsen et al, as applied to claims 1-2, 4-7, 9-12, and 34, above, and further in view of Gildea et al (US 6,485,901 B1 [26 November 2002; filed 26 October 1998]; cited in the IDS of November 2004]).

This rejection applies to claim 7 to the extent that it may be drawn to the particular type of self-reporting probe of claim 8 (i.e., to linear beacon probes).

The teachings of Ludwig et al and Hyldig-Nielsen et al are set forth in paragraph 11, above. While Hyldig-Nielsen et al teach PNA probes labeled at opposite ends with different fluorophores (see, e.g., col 11, lines 26-35), Lugwig et al and Hyldig-Nielsen et al do not specifically suggest PNA linear beacons as set forth in claim 8.

Gildea et al disclose that PNA linear beacons are "particularly well suited" for "detection, identification or quantitation" of target sequences in closed tube assays, asymmetric PCR, and in living or non-living cells, tissues and organisms (because the beacons are not degraded by enzymes) (see entire reference, particularly col 9, lines 31-58). In view of the teachings of Gildea et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the PNA probes suggested by the teachings of Ludwig et al in view of Hyldig-Nielsen et al to have included the donor and acceptor moieties required to form PNA linear beacon probes, as suggested by Gildea et al. An ordinary artisan would have been motivated to have made such a modification for the advantage of preparing a probe well-suited for any of the assays noted above, as specifically suggested by Gildea et al.

13. Claims 25-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ludwig et al in view of Hyldig-Nielsen et al, as applied to claims 1-2, 4-7, 9-12, and 34, above, and further in view of Ahern et al.

The teachings of Ludwig et al and Hyldig-Nielsen et al are set forth in paragraph 11, above. It is further noted that Hyldig-Nielsen et al teach kits comprising PNA probes "for use in diagnostics" employing the probes (see, e.g., col 20, lines 1-12), such that the combined teachings of Ludwig et al and Hyldig-Nielsen et al suggest kits comprising the probes suggested by the two references. Further, as the kits suggested by Ludwig et al in view of Hyldig-Nielsen et al could be used in any of the assays mentioned in claims 25-31 (i.e., for any of the recited intended uses of the probes/kits), the references

suggest all of the limitations of the claimed kits with the exception of the "directions" as recited in claim 25.

Ahern teaches that premade reagents provided in kit form are convenient and save researchers time and money, and further teaches the inclusion in kits of "detailed instructions to follow" (see p. 4/6). In view of the teachings of Ahern, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the kits suggested by Ludwig et al and Hyldig-Nielsen et al so as to have included therein instructions for use of the enclosed reagents. An ordinary artisan would have been motivated to have made such a modification in order to have allowed an artisan to more readily use the reagents in a correct manner, thereby saving the practitioner time and reagents, as suggested by the teachings of Ahern.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday through Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634

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